

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 02 May 2000 (02.05.00)	
International application No. PCT/NZ99/00147	Applicant's or agent's file reference 24813 MRB
International filing date (day/month/year) 03 September 1999 (03.09.99)	Priority date (day/month/year) 03 September 1998 (03.09.98)
Applicant SCHEEPENS, Arjan et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
27 March 2000 (27.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740 14 35</p>	<p>Authorized officer Nestor Santesso</p> <p>Telephone No.: (41-22) 338 83 35</p>
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT

REC'D 29 DEC 2000

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 24813 MRB	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/NZ99/00147	International Filing Date (<i>day/month/year</i>) 3 September 1999	Priority Date (<i>day/month/year</i>) 3 September 1998
International Patent Classification (IPC) or national classification and IPC Int. Cl. ⁷ A61K 38/27, 38/25		
Applicant NEURONZ LIMITED et al		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 5 sheets, including this cover sheet. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of sheet(s).
3.	This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input checked="" type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application

Date of submission of the demand 27 March 2000	Date of completion of the report 22 November 2000
Name and mailing address of the IPEA AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustria.gov.au Facsimile No. (02) 6285 3929	Authorized Officer A WILCOX Telephone No. (02) 6283 2243

I. Basis of the report1. With regard to the **elements** of the international application:*☒ the international application as originally filed.☐ the description, pages , as originally filed,
 pages , filed with the demand,
 pages , received on with the letter of☐ the claims, pages , as originally filed,
 pages , as amended (together with any statement) under Article 19,
 pages , filed with the demand,☐ the drawings, pages , as originally filed,
 pages , filed with the demand,
 pages , received on with the letter of☐ the sequence listing part of the description:
 pages , as originally filed☐ pages , filed with the demand☐ pages , received on with the letter of2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:☐ contained in the international application in written form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished4. ☐ The amendments have resulted in the cancellation of:☐ the description, pages☐ the claims, Nos.☐ the drawings, sheets fig.5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

The attorney has not commented on novelty in the response filed 10 October 2000 and the objection raised in the examiners first report is maintained.

The method of inducing a neuroprotective effect in the brain by administering growth hormone, an analog thereof or a functionally equivalent ligand to the brain lacks novelty in the light of publications cited in the International Search Report. The claims therefore do not meet the requirements for unity of invention because they do not include a common novel feature which can be considered to be a special technical feature.

Additionally a search of neuroprotective effects arising from the use of growth hormone will not establish the novelty of the use of functional analogues of growth hormone to induce a neuroprotective effect in brain tissue and the claims do not meet the requirements of unity of invention because they do not include the same special technical features.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims None	YES
	Claims 1-29	NO
Inventive step (IS)	Claims None	YES
	Claims 1-29	NO
Industrial applicability (IA)	Claims 1-29	YES
	Claims None	NO

2. Citations and explanations (Rule 70.7)

In the response filed 10 October 2000 the attorney has sought further elucidation from the examiner on the examiner's position regarding novelty and inventive step.

The examiner is in agreement with the applicant's view that none of the listed documents identifies a neuroprotective role for growth hormone (GH). The novelty and inventive step objections have been maintained because the wording of the claims includes functional analogues of growth hormones. The cited publications have been included because they disclose a neuroprotective role for functional analogues of growth hormone. The novelty and inventive step objections would be invalid if the claims were directed to methods using growth hormone or if a limiting definition for functional analogues of growth hormone were included in the specification. For example, WO 98/16242 discloses that BDNF and NGF enhance axon regeneration in sensitive neurons. EP 0357240 discloses the treatment of brain ischaemia using a polypeptide having epidermal growth factor activity.

Both publications have been cited because the use of BDNF, NGF and EGF may fall within the scope of a functional analogue of growth hormone because they are of value in a neuroprotective role. A similar comment applies to the other cited publications. Pharmaceutical formulations of growth hormone are well known.

Citations

- (a) WO 98/16242 (Regeneron Pharmaceuticals Inc.) 23 April 1998.
- (b) WO 94/23754 (The Commonwealth Of The United States of America As Represented By The Department Of Health And Human Services) 27 October 1994.
- (c) JP 2-67223 (Dia Ichi Seiyaku Co Ltd) 7 March 1990.
- (d) EP 357240 (Ethicon Inc.) 7 March 1990.
- (e) WO 91/14838 (Cephalon Inc.) 13 December 1990.
- (f) WO 93/08828 (Syntex-Synergen Neuro Science Joint Venture and The General Hospital Corporation) 13 May 1993
- (g) WO 96/40871 (Cytotherapeutics, Inc.) 19 December 1996.
- (h) WO 97/17090 (Baylor College Of Medicine) 15 May 1997.
- (i) AU 32571/97 (Boehringer Mannheim GmbH) 18 December 1997.
- (j) US 5750376 (Neurospheres Holders Ltd.) 12 May 1998.
- (k) WO 91/07947 (Ramsey Foundation) 13 June 1991.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The claims are not fairly based on the written description of the specification including the examples. The examples disclose the use of growth hormone as a neuroprotective agent in the brain. The effects of growth hormone treatment following hypoxia was detected. Cell loss in the frontoparietal cortex, the hippocampus, the striatum and thalamus were recorded. Claims to methods of treatment other than those disclosed in the examples are considered to be speculative.

The specification is not clear with respect to the description of the essential features of the invention. It is not clear what is included in the scope of the description an analog/s of growth hormones, analog/s of prolactin, analog/s of placental lactogen, functionally equivalent secretagogue/s of growth hormone releasing proteins and functionally equivalent secretagogue/s of growth hormone releasing hormone. The specification does not fully describe the invention for that reason.

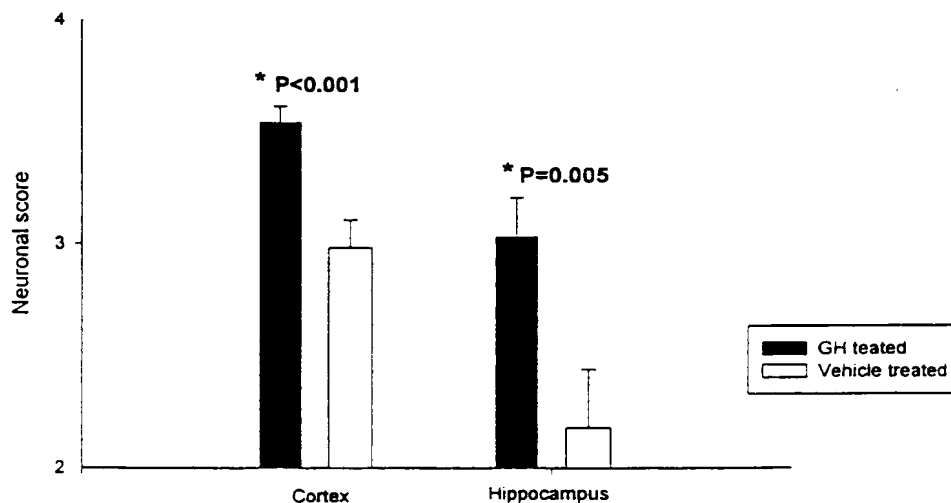


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 38/27, 38/25		A3	(11) International Publication Number: WO 00/13650
			(43) International Publication Date: 16 March 2000 (16.03.00)
(21) International Application Number: PCT/NZ99/00147 (22) International Filing Date: 3 September 1999 (03.09.99) (30) Priority Data: 331719 3 September 1998 (03.09.98) NZ (71) Applicant (for all designated States except US): NEURONZ LIMITED [NZ/NZ]; UniServices House, 58 Symonds Street, Auckland (NZ). (72) Inventors; and (75) Inventors/Applicants (for US only): SCHEEPENS, Arjan [NL/NZ]; 95 Elmore Road, RD3, Albany, Auckland (NZ). WILLIAMS, Chris, Edward [NZ/NZ]; 2/73B Carlton Gore Road, Grafton, Auckland (NZ). GLUCKMAN, Peter, David [NZ/NZ]; 78 Lucerne Road, Remuera, Auckland (NZ). CLARK, Ross, Graham [NZ/NZ]; 25 Glen Road, Devonport, Auckland (NZ). (74) Agents: BENNETT, Michael, Roy et al.; West-Walker Bennett, Mobil on the Park, 157 Lambton Quay, Wellington (NZ).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 2 June 2000 (02.06.00)	

(54) Title: NEUROPROTECTION

Effect of ICV rat GH treatment on neuronal score following moderate HI



(57) Abstract

The invention relates to neuroprotection and to medicaments for use therein. Neuroprotection is induced by activation of neural growth hormone receptors, primarily using medicaments comprising growth hormone, growth hormone analogs or ligands which are functionally equivalent. Such medicaments may also include one or more secondary neuroprotective agents.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ 99/00147

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl⁷: A61K 38/27; 38/25

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC⁶: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT: BRAIN, GROWTH HORMONE, PROLACTIN, LACTOGEN, IGF-1, GRP, activin, NGF, TGF- β , bfgf

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/16242 (Regeneron Pharmaceuticals Inc) 23 April 1998	1-29
X	WO 94/23754 (THE COMMONWEALTH OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE DEPARTMENT OF HEALTH AND HUMAN SERVICES) 27 October 1994	1-17,19,27,28,29
X	JP 2-67223 (DAI ICHI SEIYAKU CO LTD) 7 March 1990	1-18

☒ Further documents are listed in the continuation of Box C

☒ See patent family annex

* Special categories of cited documents:

"A" Document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search

14 March 2000

Date of mailing of the international search report

22 MAR 2000

Name and mailing address of the ISA/AU

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ 99/00147

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 357240 (ETHICON INC) 7 March 1990	1-18
X	WO 91/14838 (CEPHALON INC) 13 December 1990	1-29
X	WO 93/08828 (SYNTEX-SYNERGEN NEURO SCIENCE JOINT VENTURE and THE GENERAL HOSPITAL CORPORATION) 13 May 1993	1-8,24-29
X	WO 96/40871 (CYTOTHERAPEUTICS, INC) 19 December 1996	1-18
X	WO 97/17090 (BAYLOR COLLEGE OF MEDICINE) 15 May 1997	1-29
X	AU 32571/97 (BOEHRINGER MANNHEIM GmbH) 18 December 1997	1-29
X	US 5750376 (NEUROSPHERES HOLDINGS LTD) 12 May 1998	1-29
X	WO 91/07947 (RAMSEY FOUNDATION) 13 June 1991	1-29

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/NZ 99/00147

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

The method of neuroprotection in the brain by administration of growth hormone is not novel. The claims to methods using analogues of growth hormone are considered to be directed to separate inventions. The claims lack special or novel technical features.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/NZ 99/00147

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	98/16242	EP	938333				
WO	94/23754	AU	65312/94	CA	2159738	EP	696205
		US	5690927	US	5753491	US	5869463
		AU	60363/96	BR	9609154	CA	2221258
		CN	1192781	EP	832203	NZ	310048
		WO	96/39496				
JP	2-67223	JP	61143684				
EP	357240	AU	39244/89	CA	1332351	JP	2083334
		US	5057494	ZA	8905910		
WO	91/14838	AU	73633/91	CA	2057915	GB	2248248
		IT	1249409	NZ	237522	US	5299836
		FR	2659998	ZA	9101975		
WO	93/08828	AU	31297/93	US	5733871		
WO	96/40871	AU	61053/96	US	5837234		
WO	97/17090	AU	77195/96				
AU	32571/97	WO	97/47735	WO	97/47737	CN	1222191
US	5750376	AU	22425/92	CA	2113118	EP	594669
		FI	935929	NO	940056	WO	93/01275
		WO	94/16718	US	5981165	US	5750376
		US	5851832	US	5980885	AU	51474/93
		CA	2147162	EP	664832	FI	951677
		NO	951378	WO	94/09119	AU	53676/94
		AU	49241/97	EP	669973	FI	952022
		NO	951617	WO	94/10292	AU	60983/94
		CA	2155024	EP	681477	FI	953569
		NO	952985	AU	80561/94	CA	2175992
		CN	1141058	EP	728194	FI	961855
		NO	961859	WO	95/13364	AU	35152/95
		CA	2200709	EP	783693	FI	971168
		NO	971245	WO	96/09543	AU	38367/95
CONTINUED							

Patent Document Cited in Search Report		Patent Family Member					
		CN	1170435	EP	792350	FI	971956
		NO	972171	WO	96/15226	AU	38366/95
		CN	1170434	EP	792349	FI	971955
		NO	972170	WO	96/15224		
WO	91/07947	AU	69090/91	CA	2070823	EP	504263
		US	5624898				
<div>END OF ANNEX</div>							